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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,229	02/27/2002	Quin Chou	BIOS-001	6940

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EXAMINER	
KIM, YOUNG J	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 02/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application N .	Applicant(s)	
	10/087,229	CHOU ET AL.	
	Examin r	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE f this communication appears n th cover sheet with th correspondence address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,30,36,44 and 53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-20,30 and 36* is/are allowed.

6)☒ Claim(s) *44 and 53* is/are rejected.

7)☒ Claim(s) *53* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachm nt(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/24/02 & 10/22/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Preliminary Remark

The Office acknowledges the cancellation of claims 21-29, 31-35, 37-43, 45-52, and 54-60, canceled in the Preliminary Amendment received on May 24, 2002.

Priority

No priority claims is made for the instant application.

Information Disclosure Statement

The IDS(s) received on May 24, 2002 and October 22, 2003 are acknowledged and signed copies of their corresponding PTO-1449s are attached hereto.

Drawings

The drawings filed on February 27, 2002 are acceptable.

Specification

The specification is objected to because it appears to contain a typographical error. For example, on page 26, 3rd paragraph recites the phrase, "The emission intensity of donor under condition with template is divided by the emission intensity of donor under condition without template to give +/- signal ratio, which indicates *weather* the probes are degraded or not." It is believed that the italicized word, "*weather*" should be changed to "*whether.*"

Appropriate correction is required.

Claim Objections

Claim 53 is objected to because of the following informalities: Claim 53 contains a period between the improvement steps. When read in light of the specification as well as the

presence of the conjunction "or," it appears that the period is a typographical error and should be replaced with a semi-colon.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 53 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 53 is drawn to a method employing elements such as nucleic acid detector and a polymerase. However, the claim is indefinite because the claim lacks either a preamble which clearly recites what the method is for, allowing for determination of how the different elements are employed with respect to each other, or clear sub-steps disclosing how the different elements are to be employed. The instant claim only recites that it is a method comprising a nucleic acid detector and a polymerase, rendering the claim indefinite in how the elements are to be used and for what purpose.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 44 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jansen et al. (WO 03/019143 A2, published March 6, 2003, filed August 19, 2002, priority August 23, 2001) in view of Hunter et al. (US 2001/0039331 A1, published November 8, 2001, filed March 30, 2001, priority March 31, 2000).

Claim 44 is drawn to a kit comprising a i) FET labeled oligonucleotide that includes a 3'-5' exonuclease resistant quencher domain; and ii) instructions for practicing an assay.

Preliminarily, Applicants are advised that an instructional element of the kit describing its intended use is considered to be a printed matter which has no patentable weight.

Jansen et al. disclose a method of using an FET labeled oligonucleotide which includes BHQ1 at its 3' end (page 20, line 35 to page 21, line 1), wherein the oligonucleotide is a probe used in a real-time PCR assay. While Jansen et al. is not explicit in disclosing that their oligonucleotide is 3'-5' exonuclease resistant, an oligonucleotide with BHQ1 at its 3' end is determined to confer resistance to 3'-5' exonucleases according to the instant specification, wherein the instant specification discloses:

"TET labeled FET probes having ***either BHQ1*** or Eclipse Dark Quencher at 3' end are ***resistant*** to 3'→5' exonuclease, and are therefore suitable for use in high fidelity PCR..." (at page 26, bottom paragraph).

Therefore, the 3'→5' exonuclease resistance property of the oligonucleotide comprising the BHQ1 at its 3' end of Janesen et al. is considered to be an inherent property of the oligonucleotide.

Jansen et al. do not disclose that the FET oligonucleotide is comprised in a **kit** comprising an instructional material.

Hunter et al. disclose a kit [0395] comprising a probe nucleic acid labeled with FET [0169].

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to be motivated to package the FET oligonucleotide disclosed by Jansen et al. into a kit with instructions in view of the conventionality of kits in the analytical arts for the advantages of convenience, cost-effectiveness, matched and/or pre-weighed components, etc., as evidenced by Hunter et al. with a reasonable expectation of success.

"[M]ethod...may be performed, for example, by utilizing pre-packaged diagnostic kits comprising at least one probe nucleic acid... which may be conveniently used..." [0395, Hunter et al.].

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Although Jansen et al. (WO 03/019143 A2) disclose a method of conducting a polymerase chain reaction involving an FET labeled oligonucleotide having BHQ1 label at its 3' end giving an inherent 3'-5' exonuclease resistant quencher domain (page 20, line 35 to page 21, line 1), the artisans fail to make obvious or anticipate the claimed methods and the system for the following reasons.

Jansen et al., while employing the FET labeled oligonucletodie having BHQ1 label in their amplification detection method, failed to recognize that such label produced a 3'-5' exonuclease resistant labeled oligonucleotide probe. This is evident in their specification,

wherein artisans recite that their the method ***must*** only involve the use of a polymerase which has a 5'-3' exonuclease activity (page 15, lines 5-6; Jansen et al.). The use of a polymerase having a 5'-3' exonuclease activity, such as *Taq* polymerase is well known in the art of quantitative PCR, wherein the 5'-3' exonuclease function of the polymerase cleaves the FET probe to separate the attached "quencher" dye and "reporter" dye, thereby shifting the fluorescence absorption spectra, giving an indication of the formation of amplicons. Although Jansen et al. disclose a method of using an FET labeled oligonucleotide which inherently comprises a 3'-5' exonuclease resistance, the fact that artisans fail to recognize this fact is clearly evident in the polymerase employed in their disclosed method, thereby failing to motivate an ordinarily skilled artisan to conduct the method via using a polymerase 3'-5' exonuclease activity. While 3'-5' exonuclease activity in a polymerase is known in the art to be associated with a proofreading function, one of ordinary skill in the art in the art of quantitative amplification would not have had a reasonable expectation of success in using the polymerase having such a function because, absent clear knowledge that the FET labeled oligonucleotide possessed a 3'-5' exonuclease resistance, said one of ordinary skill in the art would recognized, as evidenced by instant specification, that the assay would not have worked (Table 2, see TET/Dabcyl and TET TAMRA pair resulting in degradation).

The MPEP 2143.02 states that:

"The prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success."

Therefore, because one of ordinary skill in the art, at the time the invention was made would not have been motivated nor had a reasonable expectation of success in modifying the

teachings of Jansen et al. to arrive at the claimed method of using a polymerase having a 3'-5' exonuclease activity or a system comprising the FET labeled oligonucleotide and a polymerase having 3'-5' exonuclease activity.

Claim 53 is objected to. Claims 44 and 53 are rejected.

Claims 1-20, 30, and 36 are free of prior art.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner can normally be reached from 8:30 a.m. to 6:00 p.m. Monday through Thursday. If attempts to reach the Examiner by telephone are unsuccessful, the Primary Examiner in charge of the prosecution, Dr. Kenneth Horlick, can be reached at (571) 272-0784. If the attempts to reach the above Examiners are unsuccessful, the Examiner's supervisor, Gary Benzion, can be reached at (571) 272-0782. Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (703) 872-9306. For Unofficial documents, faxes can be sent directly to the Examiner at (517) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0507.

Young J. Kim
Patent Examiner
Art Unit 1637
2/9/04